EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Refusal of a change to the marketing authorisation for Translarna (ataluren)

Re-examination confirms refusal

After re-examining its initial opinion, the European Medicines Agency has confirmed its recommendation to refuse a change to the marketing authorisation for the medicine Translarna (ataluren). The change concerned an extension of indication to add the treatment of patients with Duchenne muscular dystrophy who are no longer able to walk.

The Agency issued its opinion on 17 October 2019, after concluding the re-examination. It had issued its initial opinion on 27 June 2019.

The company that had applied for the change to Translarna's authorisation is PTC Therapeutics International Limited.

What is Translarna and what is it used for?

Translarna is a medicine used to treat patients aged 2 years and older with Duchenne muscular dystrophy who are able to walk. Duchenne muscular dystrophy is a genetic disease that gradually causes weakness and loss of muscle function. Translarna is used in the small group of patients whose disease is caused by a specific genetic defect (called a 'nonsense mutation') in the dystrophin gene.

Translarna has been authorised in the EU since July 2014. It contains the active substance ataluren and is available as granules to be taken by mouth.

Further information on Translarna's current uses can be found on the Agency's website: ema.europa.eu/medicines/human/EPAR/translarna.

What change had the company applied for?

The company applied for an extension of indication to add the treatment of patients with Duchenne muscular dystrophy who can no longer walk.

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How does Translarna work?

Patients with Duchenne muscular dystrophy lack normal dystrophin, a protein found in muscles. Because this protein helps to protect muscles from injury as muscles contract and relax, in patients with Duchenne muscular dystrophy the muscles become damaged and eventually stop working.

Duchenne muscular dystrophy can be caused by a number of genetic abnormalities. Translarna is for use in patients whose disease is due to the presence of certain defects (called nonsense mutations) in the dystrophin gene that prematurely stop the production of dystrophin, leading to a shortened dystrophin protein that does not function properly. Translarna works in these patients by enabling the protein-making apparatus in cells to move past the defect, allowing the cells to produce a functional dystrophin protein.

What did the company present to support its application?

The company provided data to show that the body handles the medicine in a similar way in patients who are able to walk and those who cannot.

In addition, the company presented the results of a study involving 94 patients with nonsense mutation Duchenne muscular dystrophy, 44 of whom were no longer able to walk. Although the main objective of the study was to assess the long-term safety of Translarna, the study also investigated the effectiveness of treatment in patients unable to walk, measuring changes in lung function. The company then compared the results with historical data from patients with Duchenne muscular dystrophy recorded in the database of the CINRG (Cooperative International Neuromuscular Research Group).

What were the main reasons for refusing the change to the marketing authorisation?

The fact that Translarna is handled by the body in a similar way in patients who can walk and those who cannot was not enough to confirm the effectiveness of Translarna in these patients. This is because patients unable to walk are at a more advanced stage of the disease and have reduced muscle mass and therefore the benefits of treatment may be different.

The additional data from the study could also not confirm the benefit of Translarna in patients no longer able to walk because there were problems with the way data from the CINRG database, which was used to indirectly compare the effects of Translarna, were selected and analysed.

Therefore, the Agency was of the opinion that the balance of benefits and risks of Translarna in patients unable to walk could not be established and recommended refusing the change to the marketing authorisation. The refusal was confirmed after re-examination.

Does this refusal affect patients in clinical trials?

The company informed the Agency that there are no consequences for patients who are receiving Translarna in clinical trials.

If you are in a clinical trial and need more information about your treatment, speak with your clinical trial doctor.

What is happening with Translarna for the treatment of patients with Duchenne muscular dystrophy who are able to walk?

There are no consequences for the use of Translarna in its authorised indication.